

occasionally ions with up to six charges have been reported. (See e.g., Dole et al., Molecular Beams of Macroions, J. Chem. Physics, vol. 49, No. 5, Sept. 1, 1968). However, not until the present invention, had molecules with up to many tens of charges been produced and identified. Thus, an important feature of the present invention is the discovery that ions of large molecules with extensive multiple charging could exist and could be readily produced. Another unique feature of the ion populations claimed in the invention is that the minimum number of charges found on any ion is always 3 or more. Whenever multiply charged ions have been found in previous studies they were always accompanied by singly and doubly charged ions.

A patent was previously granted to the coinventors of the present application on a method for producing populations of multiply charged ions and for determining molecular weights of the parent molecules by mass analysis of such charged ions. (See, U.S. Patent No. 5,130,538, Fenn et al., issued July 14, 1992)(hereinafter "Fenn II"). The present application (a divisional of the '538 patent) claims these highly multiply charged ions as a new composition of matter. The new composition of matter, as claimed, comprises sub-populations of multiply charged ions in which the minimum number of charges on each ion is greater than or equal to three and the maximum number of charges is greater than or equal to five. In addition, these populations contain at least some ions of each discrete charge state from the minimum to the maximum. Populations of ions with these characteristics have not been described or even suggested by the prior art. They do not occur in nature and had never been

produced until the coinventors, Dr. Fenn and his colleagues, carried out their experiments. Prior to their experiments, the production of populations of ions with such extensive multiple charging was unheard of.

Indeed, the production of ions with the claimed charge multiplicity (with the minimum charge per ion being greater than two, in some claims, or, greater than or equal to five in others) that Dr. Fenn et al. discovered -- with as many as 40 or more charges on a single molecule -- was an unexpected surprise and a great boon to the field of mass spectrometry. Other scientists have hailed this invention as a breakthrough. In a recent Letter to the Editor, responsive to another Letter to the Editor, one group of investigators in the field stated:

"An implication of Fernandez de la Mora's comments is that we did not sufficiently credit the remarkable achievements of Professor John Fenn and his colleagues at Yale University. If our review suggests such a view (which we believe is not the case) it is certainly incorrect! The comments upon our Review suggest that we confuse the issue of credit for the discovery of the extensive charging of macromolecules, first observed by Prof. Fenn and co-workers, and draw 'an insufficiently clear distinction between the doubly and triply charged species and the much higher states of ionization first reported in 1988 by Fenn and co-workers.' ... In our brief discussion of the history and multiple charging in ESI-MS, we point out the order in which the observations by ESI-MS were made as well as point to the significance of both the 1987 (polyethylene glycols) and 1988 (proteins) reports related to multiple charging by Fenn and co-workers. In our opinion, a key development for ESI-MS was the relatively unheralded report [by Fenn and co-workers] in 1987 of the extensive multiple charging (up to 23+) observed for polyethylene glycols. In retrospect, it is easy to say one should have immediately predicted that equivalent levels of charging should be obtainable for biopolymers. However, none of the hundreds who listened to Prof. Fenn's 1987 ASMS presentation (or read the later ASMS proceedings) and particularly none of the dozens who had access to atmospheric pressure-MS instruments (primarily Sciex TAGA's at that point) and were in a

position to extend this work to proteins (including ourselves), made this connection and conducted such experiments! What may seem straightforward in retrospect is seldom so. It takes a special genius, as demonstrated repeatedly by Prof. Fenn, to make these connections."

R.D. Smith, et al., Mass Spectrometry Reviews, vol. 11, pp 431-443 (1992).  
(Emphasis added).

In addition to the extensive degree of charging seen for the first time by Dr. Fenn and his colleagues in the ion populations they produced, certain other features of these populations are novel as well. In previous work the populations of ions that had been produced mostly comprised ions with from one to two or three charges. In one case ions with as many as six charges were produced. In those populations, singly charged ions were always present. By comparison, the populations of ions which are produced in the subject invention as claimed, contain ions with a minimum of three or more charges but contain no singly or doubly charged ions. Moreover, the ions of the claimed population have a much higher proportion of multiply charged ions than those seen in previously reported work.

The claimed discovery, in fact, has resulted in a "mini revolution" in the field of mass spectrometry. One exciting consequence, for example, is to extend the effective range of mass spectrometers far beyond their nominal upper mass limits. The molecular weight of large biomolecules of great importance in science and medicine can now be determined using low range mass spectrometers that are relatively inexpensive.

As partial evidence of the contribution of the present invention, applicants direct the Examiner's attention to the fact that, recently, Professor John B. Fenn was awarded the 1992 ASMS Award for a Distinguished Contribution in Mass Spectrometry for his work. A copy of the Announcement from the March 1992 Spectaker is attached. Moreover, two recent issues of the Journal of the American Society for Mass Spectrometers were devoted to the methods and applications of Electrospray Mass Spectrometry and were dedicated to Dr. Fenn.

Among the previous disclosures by Dr. Fenn et al. that have been cited by the Examiner, U.S. Patent No. 4,542,293, issued Sept. 17, 1985 (hereinafter "Fenn I") concerned a method for modifying the energy of ions produced in a high pressure ion source in order to meet the requirements of the mass analyzer to be used. The invention disclosed by that patent addressed the problem of producing from a source at high pressure, ions with energies sufficiently high for injection into a magnetic sector analyzer. That invention also made it possible to maintain the source of liquid sample at ground potential, so that there is no hazard to an operator. Thus, an object of Fenn I was to provide ions at any desired energy from sample sources at ground potential.

Another apparatus in the prior art, that of Labowsky et al. (See, U.S. Patent No. 4,531,056, Labowsky, Fenn & Yamashita, issued July 23, 1985) is indeed similar to that used to produce the results described in the present application. As noted by the Examiner, the ion source in the apparatus of that invention did produce populations of

multiply charged ions. However, it was universally believed, before the invention of the present application was disclosed, that any ion sources then in use could produce ions with only a limited degree of multiple charging. The discovery of this new and unique composition of matter comprised of the claimed ion populations resulted when Dr. Fenn and his colleagues' inserted pure samples of high molecular weight material into their apparatus and attempted a mass spectrometric analysis of the ions produced, despite the fact that the molecular weights of the species introduced were far beyond the nominal upper mass limit of the mass spectrometer. Previous investigators, to applicants' knowledge, had never thought to attempt the analysis of such large molecules with an analyzer having so low a mass range. Moreover, rather than disregarding the initially inexplicable findings that were produced by an experiment which, by conventional wisdom should not have been undertaken nor "worked", these inventors had the insight to analyze and understand the results they obtained and to recognize their significance. Those results comprised the first examples of the multiply charged ions that are the subject of the present application. Before the discovery by the inventors, it was universally believed that ion sources could produce only a limited degree of multiple charging. Moreover, whenever multiply charged ions had been observed, they were always accompanied by singly and doubly charged ions. Populations of ions in which all members appear to possess at least several charges had never been encountered before the experiments of Dr. Fenn and his colleagues.

In the Office Action of April 12, 1993, the Examiner relied on Fenn I in declaring anticipation of the claimed invention on grounds of "inherency". In support of this position the Examiner cited In re Fitzgerald, 205 U.S.P.Q. 594 (C.C.P.A. 1980). In that case, however, the court considered whether the product for which Fitzgerald sought a patent, namely, a self-locking, screw threaded fastener, was anticipated by a similar type of fastener patented by Barnes (with product by process claims) and cited as prior art by the Patent Office. The Patent Office, confronted in Fitzgerald's application by a product almost identical to a product which had already been patented, placed the burden on Fitzgerald to demonstrate that his product did not possess characteristics inherent in the prior Barnes product. The rationale for this shifting of the burden stems from the fact that product-by-process claims provide the Patent Office with little guidance as to the physical characteristics of such a product. Therefore, the Patent Office may require that an applicant for a product patent bear the burden of proving that the characteristics of a claimed new product are not already present or inherent in the prior art. This rationale was adopted by the Court from its earlier finding in In re Brown, 173 U.S.P.Q. 685 (1972). As the Court in Brown stated:

"It must be admitted ... that the lack of physical description in a product-by-process claim makes determination of the patentability of the [new] claim more difficult ... We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith."

In the present case, however, the highly charged ions, produced and identified by Dr. Fenn and his co-inventors were unlike anything ever previously observed or disclosed in the prior art. Neither in the practice of the invention patented by Labowsky et al., nor in any of the work of other scientists in this highly active field of research, had results such as this ever been observed and reported.

The electrospray apparatus, the subject of the '056 patent, does not inherently produce the claimed composition of matter any more than an oven inherently produced cured rubber. It took the inventive contribution of Goodrich to put natural rubber and sulphur into a prior art oven to arrive at the cured rubber. So, too, Fenn et al's contribution resides in a new composition of matter that was a product of inventive insight. The '056 apparatus was used by others for some years before the ion populations invention disclosed in the present application were even conceived, let alone actually produced and identified. See, for example, the Smith Letter to the Editor, cited on page 2, herein. It cannot be reasonably argued that the '056 apparatus inherently or inevitably leads to the claimed invention.

The doctrine of "inherency" follows one of the more fundamental principles of patent law, namely, that a party may not obtain a patent on a product which is already within the public domain. Thus, the Fitzgerald and Brown cases display a concern for preventing the patenting of a product which has already been disclosed to the public.

Prior to the discovery of the present application, however, the populations of ions that it claims are new composition of matter were not known to the public. The novelty of these ion populations is demonstrated by the fact that even skilled practicing scientists in the widely practiced area of mass spectrometry were surprised when the inventors disclosed their findings. It was Dr. Fenn and his co-inventors who first produced, identified and then reported this new composition of matter.

In fact, prior to the discovery of the present invention, not only had the claimed composition of matter never been produced, there was no evidence in the prior art that it could even exist. Multiply charged ions with limited numbers of charges had been observed but always, in the company of singly charged ions. Moreover, never had ions with as many as 40 or more charges per molecule been even encountered, let alone produced in the proportions and range of charge states that Dr. Fenn and his colleagues detected, identified, reported and now claim. Indeed, available evidence indicates that molecular ions with such extensive degrees of charging had never before been produced, even accidentally. Certainly, they had never been identified nor reported in the scientific literature. Before the reduction to practice of this invention by the inventors, there was nothing to indicate or suggest that this new composition of matter could be produced.

Even viewed with the 20-20 hindsight provided by the contributions of Dr. Fenn and his coinventors there is no evidence that any apparatus such as that of the

Labowsky-Fenn-Yamashita '056 patent, inherently could produce the multiply charged ions claimed in the present application. In the absence of any clear evidence to the contrary, speculation in hindsight that products similar to those now claimed might have been produced or inherently could be produced is surely insufficient to constitute a grounds for rejection. As the Federal Circuit has noted, "Anticipation of inventions set forth in product claims cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references". W.L. Gore & Associates v. Garlock, 220 U.S.P.Q. at 314 (Fed. Cir. 1983).

In that case, as in this one, the unique nature of the product produced, the fact that no prior art reference explicitly (or implicitly) recognized its existence and the fact that nothing in the prior art placed this new product in the possession of the public, strongly indicated that there could have been no anticipation. See, Gore 220 U.S.P.Q. at 314 ("Given the unique nature of [the claimed product], we are not persuaded that the "effect" of the processes disclosed in [the prior art], an "effect" undisclosed in those patents, would be always to inherently produce or be seen always to produce products meeting all of the claim limitations ... It is clear that the teachings of [neither prior art reference] place the product claimed in the [present] patent in possession of the public.") Also, as in that case, the advance by the present inventors resulted from proceeding in a manner utterly without precedent in recognized practice by placing pure samples of high molecular weight material into an apparatus and attempting a mass spectrometric analysis, despite the fact that the molecular weights of the sample

species were far beyond the upper limits of the mass analyzer. Such a departure from conventional practice constitutes a highly significant indication of non-anticipation. See, Gore 220 U.S.P.Q. 312 ("On the entire record and in view of all of the references, each in its entirety, it is clear that a person of ordinary skill confronted with a PTFE tape breakage problem would have either slowed the rate of stretching or increased the temperature to decrease the crystallinity. Dr. Gore did neither. He proceeded contrary to the accepted wisdom of the prior art by dramatically increasing the rate and length of stretch and retaining crystallinity. That fact is strong evidence of nonobviousness.") (citing the Supreme Court in United States v. Adams, 383 U.S. 39 (1966)).

Numerous other cases similarly indicate that even if by some chance (no evidence of which is found in any published report) the claimed product had been produced by an apparatus within the prior art, that casual production can not constitute an anticipation as long as it went unrecognized. As the Court of Customs and Patent Appeals explained: "An accidental or unwitting duplication of an invention cannot constitute an anticipation." In re Felton, 179 U.S.P.Q. at 298 (C.C.P.A. 1973). Under this doctrine, "accidental or unwitting" duplications of later-claimed inventions, which are not appreciated until the discovery by a later inventor, cannot anticipate the claimed invention. In that case, the CCPA held that a prior art reference which does not contain sufficient disclosure so as to direct one skilled in the art to the later

invention in question, can not be considered an anticipatory reference under Section 102. Id.

This doctrine is also a well established one and numerous examples arising under it and analogous to the present case may be noted. In the leading case establishing this doctrine, the Supreme Court considered a situation in which the unrecognized production of fatty acids in numerous prior art references was alleged to preclude patent protection for a later discovered process for producing free fatty acids and glycerine from fatty bodies. Finding that the prior art could not, as a matter of law, anticipate the later discovery, the Supreme Court held the following:

"We do not regard the accidental formation of fatty acid in Perkin's steam cylinder from the tallow introduced to lubricate the piston (if the scum which rose on the water issuing from the ejection pipe was fatty acid) as of any consequence in this inquiry. What the process was by which it was generated or formed was never fully understood. Those engaged in the art of making candles, or in any other art in which fatty acids are desirable, certainly never derived the least hint from this accidental phenomenon in regard to any practicable process for manufacturing such acids.

The accidental effects produced in Daniell's water barometer and in Walther's process for purifying fats and oils preparatory to soap-making, are of the same character. They revealed no process for the manufacture of fatty acids. If the acids were accidentally and unwittingly produced, whilst the operators were in pursuit of other and different results, without exciting attention and without it even being known what was done or how it had been done, it would be absurd to say that this was an anticipation of Tilghman's discovery." Tilghman v. Proctor, 102 U.S. 707, at 711-712 (1880).

Similarly in a later case, the Court considered whether the plaintiff's patent on an iron alloy known as "Adamite" was anticipated by alloys of similar analysis. The Court determined that it could not have been, finding that:

"If any of the alleged anticipating alloys was Adamite, that fact, so far as the record shows, was not known to those who produced it or used it, and not being recognized as a new product with its distinctive characteristics, its production was purely an accident without profit to the art and without value as an anticipation. We are satisfied, therefore, that Adamite has not been anticipated by alloys, which, while accidentally of the same analyses were not shown to be the 'article of manufacture' of the patent". Pittsburgh Iron & Steel Co. v. Seaman Sleeth Co., 248 F. 705, 708-9, cited in International Nickel Co., Inc. v. Ford Motor Co. 119 U.S.P.Q. 72, 80 (S.D.N.Y. 1958).

Similarly, in International Nickel Co., Inc. v. Ford Motor Co. 119 U.S.P.Q. 72, 80 (S.D.N.Y. 1958), another case analogous to the present one, the Court stated:

"It is undeniably true ... that a prior use of a product deliberately created may constitute an anticipation, though the full benefits accruing therefrom may not be fully appreciated or even recognized ... Thus if INCO had done no more than appreciate and exploit the full potentialities in a product already developed by Mack, or had merely found a new use for Mack's product, then Ford's position would have to be upheld.

Such, however, is not the situation in the instant case ... Not only was Mack unaware that it had created a new iron but in fact Mack never consciously pursued the product here in question for any purpose ... Mack never sought to manufacture nodular iron, the product which INCO has discovered. Indeed, it was unaware that it had done so ... Where the allegedly anticipating product was produced merely by chance and never recognized or appreciated, one who later discovers and recognizes the product may patent it". Id.


Recent cases speak in the same vein. See e.g. In re Felton, 179 U.S.P.Q. 295, 298 (C.C.P.A. 1973); and In re Marshall, 198 U.S.P.Q. 344, 346 (C.C.P.A. 1978).

Indeed, one recent case presents facts similar to those of the present application. There, the plaintiff, Phillips Petroleum, owned a patent for a new composition of matter, crystalline polypropylene, that had been discovered by two inventors, Hogan and Banks. When numerous parties were sued for infringement of the patent, the defendants claimed that the patent was invalid on the grounds that the compound had been inherently produced by the practice of a prior art reference. Finding that the prior patent contained no evidence to demonstrate that the prior produced product was, in fact, crystalline polypropylene, nor any evidence which would have led one skilled in the art to the conclusion that a new form of polypropylene had been produced, the court found that the prior patent could not anticipate the later one. See, Phillips Petroleum Co. v. U.S. Steel Corp., 6 U.S.P.Q.2d 1065 (D. Delaware 1987). ("As Phillips notes, the [prior] patent does not disclose ... [any] measurements that might have led one skilled in the art to conclude that the patentee had discovered what would have been, in 1951, a wholly new and different form of polypropylene." *Id.* at 1076). The Court placed further significance on the fact that "prior to the invention of Hogan and Banks' [of crystalline polypropylene], there was no reason for polymer chemists to predict that crystalline polypropylene could even be produced". *Id.* at 1095. During the period of the prior patent, "chemists at the time simply did not know whether the production of crystalline polypropylene was even possible". *Id.* at 1094. Indeed, "the [prior] patent did not describe to the man of ordinary skill in the art ... how to go about producing crystalline polypropylene. A person of ordinary skill in the art would not find crystalline polypropylene to be an obvious product of that [prior]

patent, nor would one be led to produce that product as a result of the [prior] patent".  
Id. at 1101. Here, as in Phillips, where before the present discovery scientists in this field did not even know whether the ion populations claimed in the present application could exist, and where nothing in the prior art referred to populations of multiply charged ions of the claimed charge states, it is clear that the subject of the present claims has not been anticipated.

In view of these previous rulings by the court, the applicants believe that the absence of relevant prior art in this field and the applicable law provide sufficient justification for the present application to pass to issue. Applicants respectfully request favorable action on the merits.

Respectfully submitted,

  
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# SPECTAKER

The American Society for Mass Spectrometry \* P. O. Box 1508, East Lansing, MI 48826 \* (517) 337-2548 \* March, 1992

## The 1992 ASMS AWARD for a DISTINGUISHED CONTRIBUTION in MASS SPECTROMETRY



**Professor JOHN B. FENN**

*for the development of Electrospray Mass Spectrometry*

In a series of papers beginning in 1984, John Fenn and his collaborators at Yale University described and applied a new principle of sample introduction and ionization for mass analysis, known as electrospray mass spectrometry. This innovative achievement has had a very significant effect on the practice of mass spectrometry by extending the mass range and type of compounds that can be analyzed by conventional instrumentation.

Prior to electrospray, most ionization techniques resulted in the production of singly charged ions in which 2,000-10,000 daltons defined the outer limits for quadrupole and magnetic mass analyzers. With electrospray ionization, charge (either positive or negative) is associated with each functional group in a molecule based upon its solution chemistry. For proteins with molecular weights of 100-200,000, it is common to measure 30-50 charges per molecule using conventional instrumentation with mass assignment accuracy of 100 ppm. Because electrospray ionization is inherently a solution technique, it has found immediate application in biopolymer analysis, especially when coupled to chromatographic separations.

The development of Dr. Fenn's electrospray technique has had a significant impact on mass spectrometry, and its application will have a profound influence upon physico-chemical measurement techniques, in fields such as fundamental chemistry, biochemistry, immunology, and genetics.

## CONFERENCE NEWS

The meeting in Washington will feature plenaries, orals, and symposia in the morning; workshops, introductory lectures on lasers and molecular biology, as well as a symposium on fullerenes, in the afternoon. Posters, including a meeting-within-a-meeting poster session on PDMS, will be displayed all day. The evenings are free to roam the suites and see Washington, but don't forget the Corporate Poster Session on Tuesday evening.

**WORKSHOPS:** A listing of workshops appears in the Preliminary Program. Note the two introductory workshops on Tuesday afternoon: An Introduction to Lasers in Mass Spectrometry, presented by Steve Leone, University of Colorado and An Introduction to Molecular Biology by William DeLorbe, Executive Director of Biotechnology with DuPont Merck Pharmaceuticals.

**REGISTRATION:** Advance registration for the Conference will continue to be accepted if RECEIVED by April 24. In order to receive the program on diskette; however, your registration must have been received by February 28. For those who do not register by April 24, there will be on-site registration beginning at 3 pm at the Hilton Hotel. The cost of on-site registration is \$20 more than the advance fee. To register as a member, 1992 dues must be paid by March 30.

**ACCOMMODATIONS:** All conference sessions will be held at the Washington Hilton Hotel & Towers. Sleeping rooms at the Hilton are \$101 (single) and \$113 (double). You can make reservations by calling the Hilton at (202) 483-3000.

**HIGHLIGHTS:** Wednesday morning the recipient of 1992 ASMS Award for Distinguished Contribution to Mass Spectrometry will present a plenary lecture. The Research Awards sponsored by Finnigan and VG will be announced.

## Mass Spectra: How to Label and Scale the Horizontal Axis

Alan G. Marshall

The increasing interest in multiply charged ions highlights the need for a uniform convention for labeling and scaling of mass spectra, as noted in an ASMS workshop chaired by Alan Rockwood. His analysis was discussed at the latest ASMS board meeting, where it was agreed that the first priority should be that **mass-to-charge ratio should be reported in correct units, namely, Da/e, or equivalently, u/e**, in which the dalton (Da) or atomic mass unit (u) is defined as 1/12 of the mass of a single (neutral)  $^{12}\text{C}$  atom, and e is the elementary charge (i.e., electrostatic charge of one electron). A separate issue is whether or not to assign a new name ("thomson") to "u/e". Advantages of the "thomson" are compact notation and automatically correct units for mass spectra. The main disadvantage is the removal by one mental step of the recognition that the "thomson" is itself a ratio (e.g., we don't have a separate unit for velocity, which is correctly reported as m/s).

A related issue is how to label the mass spectral abscissa. Clearly, "mass" or "m" is inappropriate. One precise label would be "mass-to-charge ratio". Choices, such as "m/z", "m/ze", or "m/q", depend on prior definition of "m", "z", and "q". Of these, "m/z" is most commonly used, but presents the disadvantage that its units are not obvious without accompanying definition. Other choices might be "m/ze" (in which "m" is ionic mass, "z" is the number of charges per ion), or "m/q" (in which "q" is ionic charge).

In summary, the ASMS board recommends that the mass spectral axis should be labeled unambiguously (e.g., "mass-to-charge ratio" or a formula with appropriately defined terms).

## ASMS CALENDAR

1992

**March 30:** Deadline for 1992 dues to qualify for member rate at conference.

**April 24:** Deadline for receipt of ASMS Short Course registration & advance Conference registration

**May 30-31:** ASMS Short Courses, Washington, DC.

**May 31-June 5:** The 40th ASMS Conference on Mass Spectrometry, Washington, DC.

**Sept. 27-Oct. 1:** The 9th Asilomar Conference on Mass Spectrometry, "Trapped Ions: Principles, Instrumentation & Applications.

Program Chairs: R. Graham Cooks and Alan G. Marshall. Contact: Laszlo Tokes (415) 855-5713.

**Nov. 20-21:** ASMS Fall Workshop, Electrospray II. Westin Hotel, Copley Place Boston.

1993

**Jan. 23-26:** Sanibel Conference on Carbohydrates.

## FRONTIERS IN IMMUNOLOGY

Vernon Reinhold

In an effort to appreciate new applications and research areas in need of analytical support, a symposium has been organized to enlighten, challenge, and stimulate all. "Frontiers In Immunology" is scheduled for Thursday morning of Conference week (9:30 am - 1:30 pm). Two leading immunologists, Professors Leroy Hood and Elis. Reinherz, will outline current developments and the impending challenges in an area that touches us all. Dr. Hood is Boles Professor of Biology at Caltech and known to many for his major contributions in developing automated microchemical instrumentation. Dr. Reinherz is Chief of the Laboratory of Immunobiology, Dana-Farber Cancer Institute and Professor of Medicine at Harvard Medical School. A published report recently found that Dr. Reinherz's laboratory received the highest number of citations in 1989.

A more direct focus on specific problems will be provided by Professor Patrick Brennen (Colorado State University), a specialist in disease-causing parasites (*Mycobacterium* sp), and two contributing mass spectroscopists, Don Hunt (University of Virginia) and Vern Reinhold (Harvard University). They will discuss detailed aspects of cellular immunology, antigen processing, and the ubiquitous involvement of carbohydrate structures in these processes.

The relentless prokaryote-eukaryote battle for survival, organ transplant, and cellular auto-immune diseases are topics of great importance. An understanding of these fundamental processes at the structural level is just beginning. As mass spectroscopists, are we ready to undertake the challenge?

### Kyoto '92 Conference

on

### Biological Mass Spectrometry

September 20-24, 1992

Travel Funds are available  
jointly sponsored by  
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